

Amendments to the Claims:

1. - 99. (Canceled)

100. (New) A continuous method of forming particles comprising the following steps:

- (a) providing an aqueous solution comprising coprecipitant molecules and bioactive molecules, each coprecipitant molecule substantially having a molecular weight of less than 4kDa, wherein the aqueous solution is capable of forming a coprecipitate which comprises the coprecipitant and bioactive molecules with a melting point of above about 90°C;
- (b) rapidly admixing the bioactive molecule/coprecipitant molecule solution with a greater volume of a substantially water miscible organic solvent such that the coprecipitant and bioactive molecules coprecipitate from solution forming said particles; and
- (c) optionally isolating the particles from the organic solvent.

101. (New) A method according to claim 100, wherein following mixing with the bioactive molecule the coprecipitant will be at between about 5 and 100 % or between about 20 and 80 % of its aqueous saturation solubility.

102. (New) A method according to claim 100, wherein the coprecipitant has a substantially lower solubility in the miscible organic solvent than in the aqueous solution.

103. (New) A method according to claim 100, wherein an excess of fully water miscible organic solvent is such that the final water content of the solvent/aqueous solution is generally less than about 30 vol%, less than about 10-20 vol% or less than about 8 vol%.

104. (New) A method according to claim 100, wherein the water miscible organic solvent is selected from any of the following: methanol; ethanol; propan-1-ol; propan-2-ol; acetone, ethyl lactate, tetrahydrofuran, 2-methyl-2,4-pentanediol, 1,5-pentanediol, and various size polyethylene glycol (PEGs) and polyols; or any combination thereof.

105. (New) A method according to claim 100, wherein the organic solvent is pre-saturated with the bioactive molecule and/or coprecipitate to ensure that on addition and mixing of the aqueous solution the two components precipitate out together.

106. (New) A method according to claim 100, wherein the aqueous phase is added slowly to a large excess of the solvent phase and a mixing process that is turbulent or near turbulent is used.

107. (New) A method according to claim 100, wherein the aqueous solution is added to organic solvent as a continual stream, spray or mist.

108. (New) A method according to claim 100, wherein a water miscible organic solvent or mixture of solvents is continuously flowed and mixed with a slower flowing aqueous stream comprising a bioactive molecule and coprecipitant solution producing a combined output flow that contains suspended bioactive molecule coated microcrystal particles.

109. (New) A method according to claim 100, wherein upon admixing the bioactive molecule/coprecipitant solution to the excess of the water miscible organic solvent, precipitation of the bioactive and coprecipitant occurs substantially instantaneously.

110. (New) Particles as formed according to claim 100.

111. (New) Particles obtainable by:

- (a) providing an aqueous solution comprising coprecipitant molecules and bioactive molecules, each coprecipitant molecule substantially having a molecular weight of less than 4kDa, wherein the aqueous solution is capable of forming a coprecipitate which comprises the coprecipitant and bioactive molecules with a melting point of above about 90°C;
- (b) rapidly admixing the bioactive molecule/coprecipitant molecule solution with a greater volume of a substantially water miscible organic solvent

such that the coprecipitant and bioactive molecules coprecipitate from solution forming said particles; and

- (c) optionally isolating the particles from the organic solvent.

112. (New) A pharmaceutical formulation comprising particles wherein the particles comprise:

- (a) a substantially non-hygroscopic inner crystalline core comprising coprecipitant molecules wherein said coprecipitant molecules have a molecular weight of less than 4kDa; and
- (b) an outer coating comprising one or more bioactive molecules wherein the particles have been formed in a single step by coprecipitating said core forming coprecipitant molecules and said bioactive molecule(s) together and wherein the particles have a melting point of above about 90°C.

113. (New) A pharmaceutical formulation according to claim 112, wherein the molecules forming the crystalline core have a solubility in water of less than about 150 mg/ml or less than about 80 mg/ml.

114. (New) A pharmaceutical formulation according to claim 112, wherein the molecules which make up the crystalline core are selected from any of the following: amino acids, zwitterions, peptides, sugars, buffer components, water soluble drugs, organic and inorganic salts, compounds that form strongly hydrogen bonded lattices or derivatives or any combinations thereof.

115. (New) A pharmaceutical formulation according to claim 112, wherein bioactive molecules forming a coating on the crystalline core are selected from any molecule capable of producing a therapeutic effect such as an active pharmaceutical ingredient (API).

116. (New) A pharmaceutical formulation according to claim 112, wherein the coating of bioactive molecules also comprises excipients commonly used in pharmaceutical formulations such as stabilizers, surfactants, isotonicity modifiers and pH/buffering agents.

117. (New) A pharmaceutical formulation according to claim 112, wherein the bioactive molecules comprise: any drug, peptide, polypeptide, protein, nucleic acid, sugar, vaccine component, or any derivative thereof or any combination which produces a therapeutic effect.

118. (New) A pharmaceutical formulation according to claim 112, wherein the bioactive molecules comprise: anti-inflammatories, anti-cancer agents, anti-psychotic agents, anti-bacterial agents, anti-fungal agents; natural or unnatural peptides; proteins such as insulin,  $\alpha$ 1-antitrypsin,  $\alpha$ -chymotrypsin, albumin, interferons, antibodies; nucleic acids such as fragments of genes, DNA from natural sources or synthetic oligonucleotides, anti-sense nucleotides and RNA; and sugars such as any mono-, di- or polysaccharides; and plasmids.

119. (New) A pharmaceutical formulation according to claim 112, wherein vaccine coating components include antigenic components of a disease causing agent, such as a bacterium or virus, such as diphtheria toxoid and/or tetanus toxoid.

120. (New) A pharmaceutical formulation according to claim 120, wherein the vaccine components are sub-unit, attenuated or inactivated organism vaccines such as diphtheria, tetanus, polio, pertussis and hepatitis A, B and C, HIV, rabies and influenza.

121. (New) A pharmaceutical formulation according to claim 120, wherein the vaccine is diphtheria toxoid coated D,L-valine or L-glutamine crystals.

122. (New) A pharmaceutical formulation according to claim 112, wherein the particles are also applicable to administration of polysaccharides linked to proteins such as HiB (haemophilus influenza B) and pneumococcal vaccines and live virus vaccines, such as mumps, measles, rubella and modern flu vaccine components such as MV A vectored influenza vaccine.

123. (New) A pharmaceutical formulation according to claim 112, wherein vaccine component coated micro-crystals are used for formulation of vaccines developed for cancers, especially human cancers, including melanomas, skin cancer, lung cancer, breast cancer, colon cancer and other cancers.

124. (New) A pharmaceutical formulation according to claim 112, wherein the particles are selected from the following: a crystalline core of valine and a coating of insulin; a crystalline core of glycine and a coating of antitrypsin, a crystalline core of Na glutamate and a coating of insulin; a crystalline core of methionine and a coating of insulin; a crystalline core of alanine and a coating of insulin; a crystalline core of valine and a coating of insulin; a crystalline core of histidine and a coating of insulin; a crystalline core of glycine and a coating of  $\alpha$ -antitrypsin; a crystalline core of glutamine and a coating of albumin; a crystalline core of valine and a coating of oligonucleotides DQA-HEX; a crystalline core of valine and a coating of  $\alpha$ 1-antitrypsin with a further anti-oxidant outer coating of N-acetyl cystein; a crystalline core of valine and a coating of ovalbumin; a crystalline core of glutamine and a coating of ovalbumin, a crystalline core of valine and a coating of diptheria taxoid; a crystalline core of glutamine and a coating of diptheria taxoid; a crystalline core of valine and a coating of diptheria taxoid; a crystalline core of the glutamine and a coating of tetanus taxoid; a crystalline core of the valine and a coating of a mixture of diptheria taxoid and tetanus taxoid; a crystalline core of glutamine and a coating of a mixture of diptheria taxoid and tetanus taxoid.

125. (New) A pharmaceutical formulation according to claim 112, wherein following exposure to temperature of up to 60°C for 1 week and reconstitution in aqueous solution the bioactive molecule retains a biological activity substantially similar to that of a freshly prepared formulation.

126. (New) A pharmaceutical formulation according to claim 112, wherein the formulation is delivered to a recipient by parenteral, pulmonary, nasal, sublingual, intravenous, rectal, vaginal, intra-anal or oral administration.

127. (New) A pharmaceutical formulation according to claim 112, comprising a dry powder of bioactive molecule coated microcrystals with a bulk density of less than about 0.3g/ml or less than about 0.1 g/ml.

128. (New) A pharmaceutical formulation for pulmonary delivery comprising particles according to claim 100.

129. (New) A pharmaceutical formulation according to claim 129, wherein bioactive molecules suitable for the formation of pulmonary pharmaceutical formulations include any of the following: therapeutic proteins such as insulin,  $\alpha$ 1-antitrypsin, interferons; antibodies and antibody fragments and derivatives; therapeutic peptides and hormones; synthetic and natural DNA including DNA based medicines; enzymes; vaccine components; antibiotics; pain-killers; water-soluble drugs; water-sensitive drugs; lipids and surfactants; polysaccharides; or any combination or derivatives thereof.

130. (New) A pharmaceutical formulation according to claim 129, wherein the pulmonary formulation comprising particles are used directly in an inhaler device to provide high emitted doses and high fine particle fractions.

131. (New) A pharmaceutical formulation according to claim 129, wherein for pulmonary formulations, the particles have a mass median aerodynamic diameter less than about 10 microns, less than about 5 microns or less than about 3.5 microns.

132. (New) A pharmaceutical formulation according to claim 129, wherein pulmonary formulations are selected to have crystalline cores comprised of amino-acids such as valine, histidine, isoleucine, glycine or glutamine.

133. (New) A pharmaceutical formulation according to claim 129, wherein the pulmonary formulations are selected from any of the following: a crystalline core of valine and a coating of a therapeutic protein such as insulin; a crystalline core of histidine and a coating of an enzyme; a crystalline core of valine and a coating of an enzyme inhibitor such as  $\alpha$ -antitrypsin; a

crystalline core of valine and a coating of DNA; a crystalline core of valine and a vaccine coating; and a crystalline core of glutamine and a vaccine coating; a crystalline core of glutamine and a coating of albumin.

134. (New) A parenteral formulation comprising particles or suspensions of particles according to claim 100.

135. (New) A sustained or controlled release pharmaceutical formulation (or a depots) comprising particles or suspensions of particles according to claim 100.

136. (New) Use of particles according to claim 100 in the manufacture of a medicament wherein the medicament is administered in a pulmonary, parenteral, nasal, sublingual, intravenous, rectal, vaginal, intra-anal or oral administration, for use in therapy.